PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 202.13 WO	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US03/27186	International filing date *(day/month/year)* 28 August 2003 (28.08.2003)	Priority date *(day/month/year)* 28 August 2002 (28.08.2002)
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 31/56 and US Cl.: 514/177, 178, 182		
Applicant HOLLIS-EDEN PHARMACEUTICALS, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 27 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
03 March 2004 (03.03.2004)	20 December 2004 (20.12.2004)
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Raymond J. Henley III Telephone No. 571-272-0600

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/27186

I. Basis of the report

1. With regard to the **elements** of the international application:*

☐ the international application as originally filed.

☒ the description:
pages 1-356 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the claims:
pages NONE, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages 357-383, filed with the demand
pages NONE, filed with the letter of _____.

☐ the drawings:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☐ the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE

☐ the claims, Nos. NONE

☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/27186

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 1-44	YES
	Claims NONE	NO
Inventive Step (IS)	Claims 1-44	YES
	Claims NONE	NO
Industrial Applicability (IA)	Claims 1-44	YES
	Claims NONE	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-44 meet the criteria under PCT Article 33(2) for novelty because the prior art fails to teach the presently claimed use of the claimed compounds for the treatment of cystic fibrosis, autism, sickle cell disease, neutropenia or thrombocytopoenia; the presently claimed method to treat or reduce the severity of a chronic allergy or an atopic disease, or the symptoms thereof which comprises the administration of the claim designated compounds to a subject in need thereof; the present presently claimed method to modulate the expression in a cell of the level of or an activity of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more gene products or gene transcripts; the presently claimed pharmaceutical composition comprising a compound as defined in the present claims; the presently claimed use of the claimed compounds for the treatment of a delayed adverse effect, symptom or condition from ionizing radiation exposure in a subject; or the presently claimed use of a compound for the treatment of an immune suppression condition or an unwanted inflammation or autoimmune condition in a subject.

Claims 1-44 meet the criteria under PCT Article 33(3) for inventive step because the prior art fails to teach or suggest the presently claimed use of the claimed compounds for the treatment of cystic fibrosis, autism, sickle cell disease, neutropenia or thrombocytopoenia; the presently claimed method to treat or reduce the severity of a chronic allergy or an atopic disease, or the symptoms thereof which comprises the administration of the claim designated compounds to a subject in need thereof; the present presently claimed method to modulate the expression in a cell of the level of or an activity of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more gene products or gene transcripts; the presently claimed pharmaceutical composition comprising a compound as defined in the present claims; the presently claimed use of the claimed compounds for the treatment of a delayed adverse effect, symptom or condition from ionizing radiation exposure in a subject; or the presently claimed use of a compound for the treatment of an immune suppression condition or an unwanted inflammation or autoimmune condition in a subject.

Claims 1-44 meet the criteria under PCT Article 33(4) because the presently claimed use of the claimed compounds for the treatment of cystic fibrosis, autism, sickle cell disease, neutropenia or thrombocytopoenia; the presently claimed method to treat or reduce the severity of a chronic allergy or an atopic disease, or the symptoms thereof which comprises the administration of the claim designated compounds to a subject in need thereof; the present presently claimed method to modulate the expression in a cell of the level of or an activity of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more gene products or gene transcripts; the presently claimed pharmaceutical composition comprising a compound as defined in the present claims; the presently claimed use of the claimed compounds for the treatment of a delayed adverse effect, symptom or condition from ionizing radiation exposure in a subject; and the presently claimed use of a compound for the treatment of an immune suppression condition or an unwanted inflammation or autoimmune condition in a subject would each have applicability in the medical industry.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

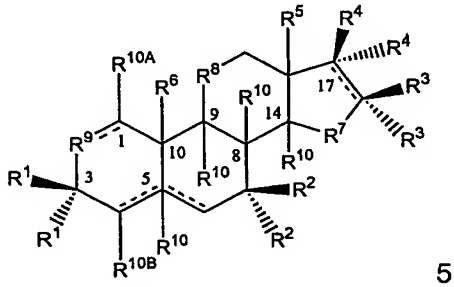
Claims 1-26, 28, 29, 35-44 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the claims are indefinite for the following reason:

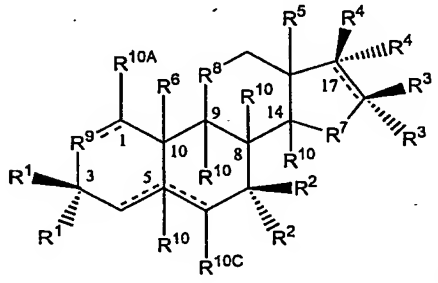
The term "use" does not particularly point out any specific manipulative step to be performed in order to accomplish the claimed objectives.

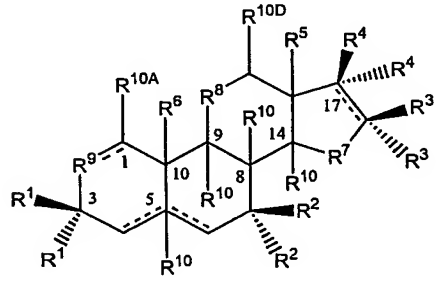
CLAIMS

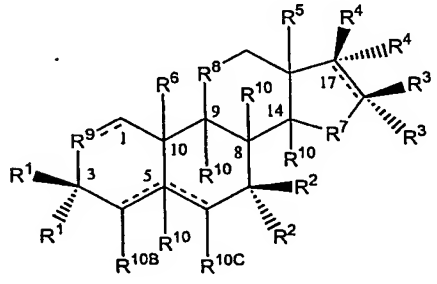
[00932] What is claimed is:

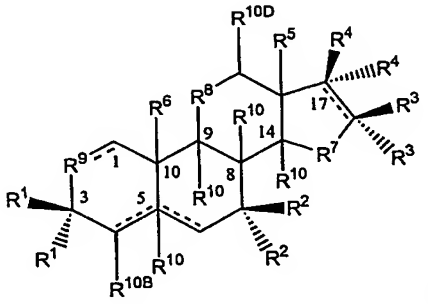
[00933] 1. Use of a compound for the treatment of cystic fibrosis, autism, sickle cell disease, neutropenia or thrombocytpoenia in a subject, or for the treatment of a symptom of neutropenia or thrombocytopenia, wherein the compound has the structure 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14

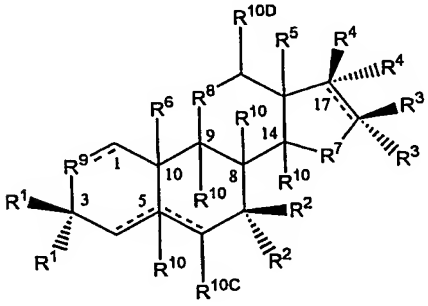
[00934]  5,

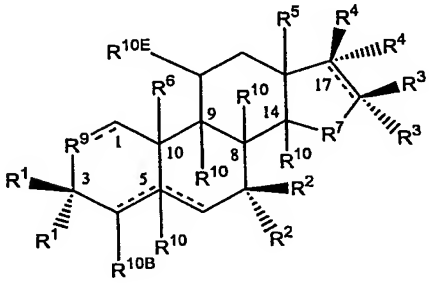
[00935]  6,

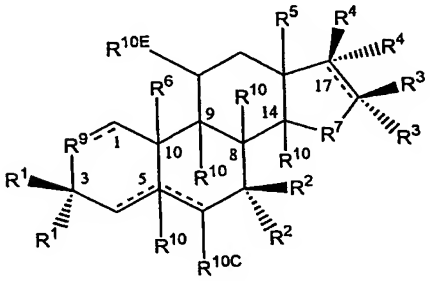
[00936]  7,

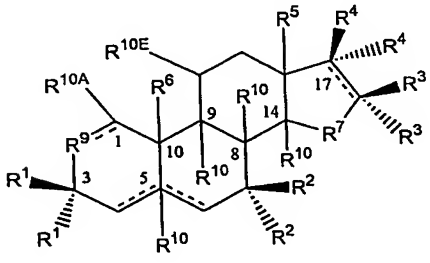
[00937]  8,

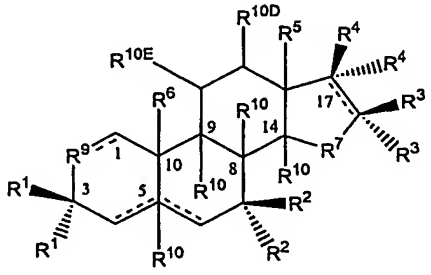
[00938]  9,

[00939]  10,

[00940]  11,

[00941]  12,

[00942]  13 or



[00943] 14,

[00944] or a salt, metabolic precursor or a metabolite thereof, wherein

[00945] R^{10} moieties at the 5 (if present), 8, 9 and 14 positions respectively are in the α,α,α,α, α,α,α,β, α,α,β,α, α,β,α,α, β,α,α,α, α,α,β,β, α,β,α,β, β,α,α,β, β,α,β,α, β,β,α,α, α,β,β,α, α,β,β,β, β,α,β,β, β,β,α,β, β,β,β,α or β,β,β,β configurations,

[00946] wherein R^{10A}, R^{10B}, R^{10C}, R^{10D} and R^{10E} respectively are in the α,α, α,β, β,α or β,β configurations,

[00947] wherein, each R^1, R^2, R^3, R^4, R^5, R^6, R^{10}, R^{10A}, R^{10B}, R^{10C}, R^{10D} and R^{10E} independently are -H, -OH, -OR^{PR}, -SR^{PR}, -NHR^{PR}, -$N(R^{PR})_2$, -O-Si-$(R^{13})_3$, -CHO, -CHS, -CN, -SCN, -NO_2, -NH_2, -COOH, -OSO_3H, -OPO_3H, an ester, a thioester, a thionoester, a phosphoester, a phosphothioester, a phosphonoester, a phosphiniester, a sulfite ester, a sulfate ester, a sulfamate, a sulfamide, a sulfonamide, a sulfurous diamide, an amide, an amino acid, a peptide, an ether, a thioether, an acyl group, a thioacyl group, a carbonate, a carbamate, a halogen, an optionally substituted alkyl group, an optionally substituted alkenyl group, an optionally substituted alkynyl group, an optionally substituted aryl moiety, an optionally substituted heteroaryl moiety, an optionally substituted heterocycle, an optionally substituted monosaccharide, an optionally substituted oligosaccharide, a nucleoside, a nucleotide, an oligonucleotide, a polymer, or,

[00948] one more of R^1, R^2, R^3, R^4, R^5, R^6, R^{10}, R^{10A}, R^{10B}, R^{10C}, R^{10D} and R^{10E} are =O, =S, =N-OH, =CH_2, =CH-CH_3, or an independently selected spiro ring and the hydrogen atom or the second variable group that is bonded to the same carbon atom is absent, or,

[00949] one or more of two adjacent R^1-R^6, R^{10}, R^{10A}, R^{10B}, R^{10C}, R^{10D} and R^{10E} comprise an independently selected epoxide, acetal, a thioacetal, ketal or thioketal;

[00950] R^7 is -$C(R^{10})_2$-, -$C(R^{10})_2$-$C(R^{10})_2$-, -$C(R^{10})_2$-$C(R^{10})_2$-$C(R^{10})_2$-, -$C(R^{10})_2$-O-$C(R^{10})_2$-, -$C(R^{10})_2$-S-$C(R^{10})_2$-, -$C(R^{10})_2$-NR^{PR}-$C(R^{10})_2$-, -O-, -O-$C(R^{10})_2$-, -S-, -S-$C(R^{10})_2$-, -NR^{PR}- or -NR^{PR}-$C(R^{10})_2$-;

[00951] R^8 and R^9 independently are $-C(R^{10})_2-$, $-C(R^{10})_2-C(R^{10})_2-$, -O-, $-O-C(R^{10})_2-$, -S-, $-S-C(R^{10})_2-$, $-NR^{PR}-$ or $-NR^{PR}-C(R^{10})_2-$, or one or both of R^8 or R^9 independently are absent, leaving a 5-membered ring;

[00952] R^{13} independently is C_{1-6} alkyl; and

[00953] R^{PR} independently is -H or a protecting group, provided that (1) one R^4 is $-NH_2$, an optionally substituted amine, $-N(R^{PR})^2$, =NOH, =NO-optionally substituted alkyl, an amide or an N-linked amino acid, or (2) the condition is cystic fibrosis or a sickle cell disease.

[00954] 2. Use according to claim 1 wherein one each of R^1, R^2, R^3 and R^4 are -H, and, when no double bond links the second R^1, R^2, R^3 and R^4 to the ring to which it is bonded and no double bond is present at the 16-17 position, then the second R^1, R^2, R^3 and R^4 respectively are in the α,α,α,α, α,α,α,β, α,α,β,α, α,β,α,α, β,α,α,α, α,α,β,β, α,β,α,β, β,α,α,β, β,α,β,α, β,β,α,α, α,β,β,α, α,β,β,β, β,α,β,β, β,β,α,β, β,β,β,α or β,β,β,β configurations and the second R^1, R^2, R^3 and R^4 are optionally independently selected from -H, -F, -Cl, -Br, -I, -OH, -SH, $-NH_2$, -COOH, $-CH_3$, $-C_2H_5$, $-C(CH_3)_3$, $-OCH_3$, $-OC_2H_5$, $-CF_3$, $-CH_2OH$, $-C(O)CH_3$, $-C(O)CH_2OH$, $-C(O)CH_2F$, $-C(O)CH_2Cl$, $-C(O)CH_2Br$, $-C(O)CH_2I$, $-C(O)CF_3$, $-C_2F_5$, =O, $=CH_2$, $=CHCH_3$, amino acid, carbamate, carbonate, optionally substituted C1-C20 alkyl, optionally substituted C1-C20 ether, optionally substituted C1-C20 ester, optionally substituted C1-C20 thioether, optionally substituted C1-C20 thioester, optionally substituted monosaccharide, optionally substituted disaccharide, optionally substituted oligosaccharide.

[00955] 3. Use according to claim 1 or 2 wherein

[00956] (a) R^{10A} is bonded to the ring to which it is attached by a single bond and a double bond is present at (i) the 1-2 position, or (ii) the 1-2 and 16-17 positions; or

[00957] (b) R^{10B} is bonded to the ring to which it is attached by a single bond and a double bond is present at the 4-5 position; or

[00958] (c) R^{10c} is bonded to the ring to which it is attached by a single bond and a double bond is present at the 5-6 position; or

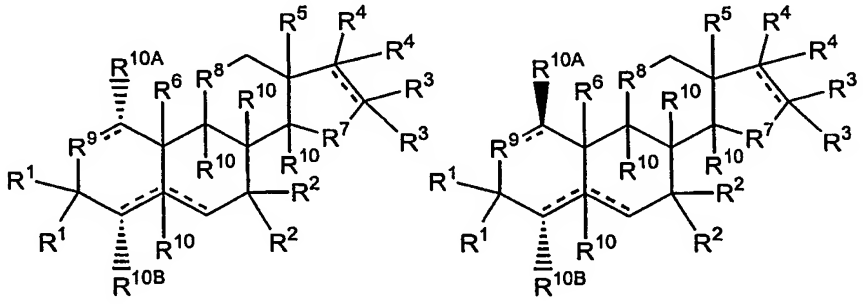
[00959] (d) R^{10A} and R^{10B} are bonded to the rings to which they are attached by a single bond and a double bond is present at (i) the 1-2 and 4-5 positions, or (ii) the 1-2, 4-5 and 16-17 positions;

[00960] (e) R^{10A} and R^{10C} are bonded to the rings to which they are attached by a single bond and a double bond is present at (i) the 1-2 and 5-6 positions, or (ii) the 1-2, 5-6 and 16-17 positions; or

[00961] (f) no double bond is present.

[00962] 4. Use according to claim 3 wherein the compounds of structure 5, 6, 7, 8, 9, 10, 11 and 12 have the structure

[00963]



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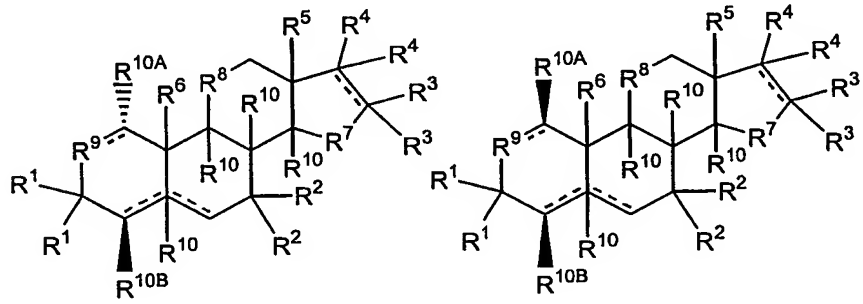

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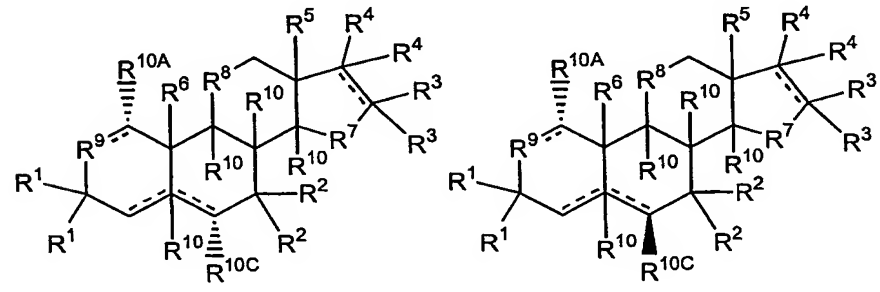
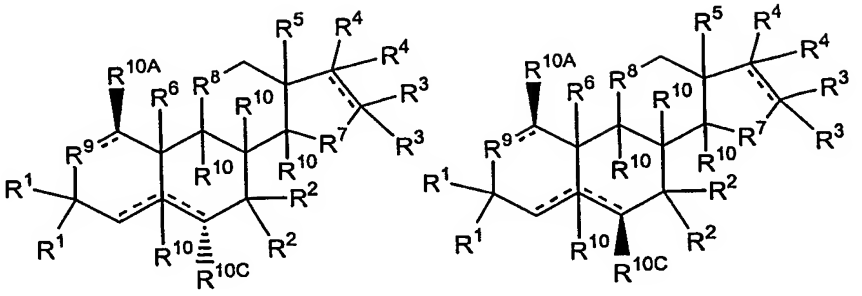
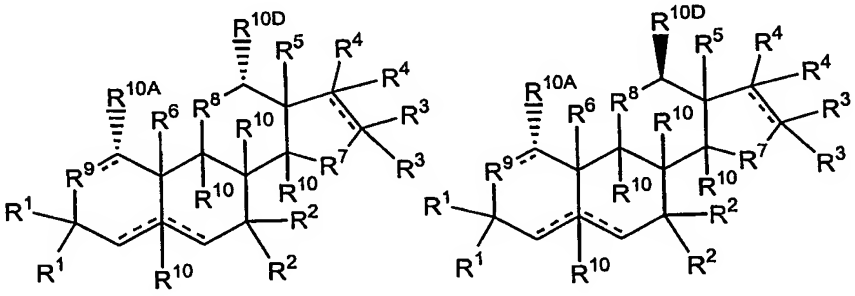
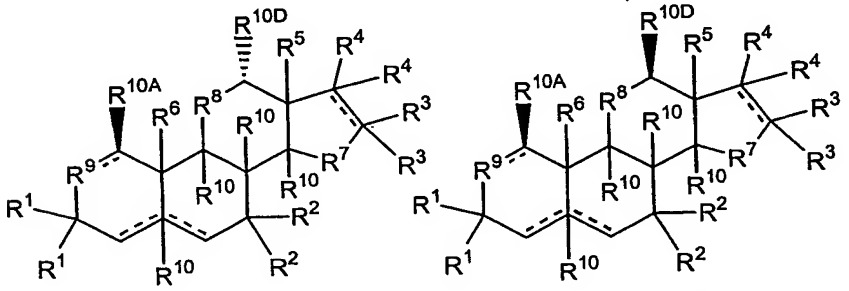
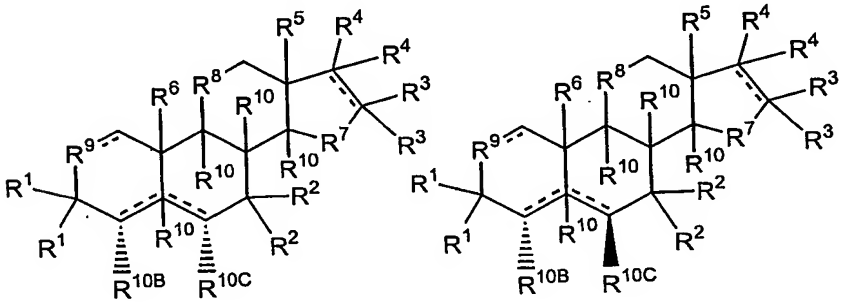
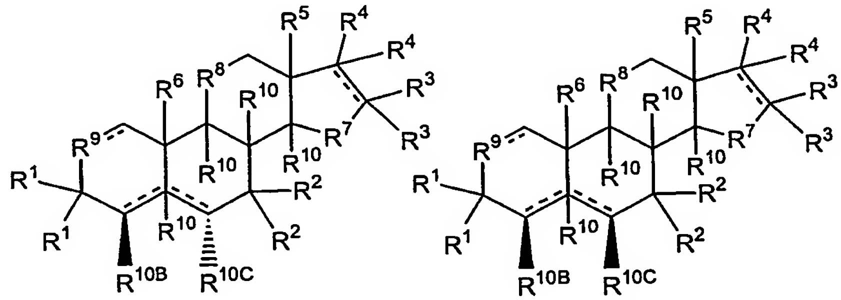


[00966] 

[00967] 

[00968] 

[00969] 



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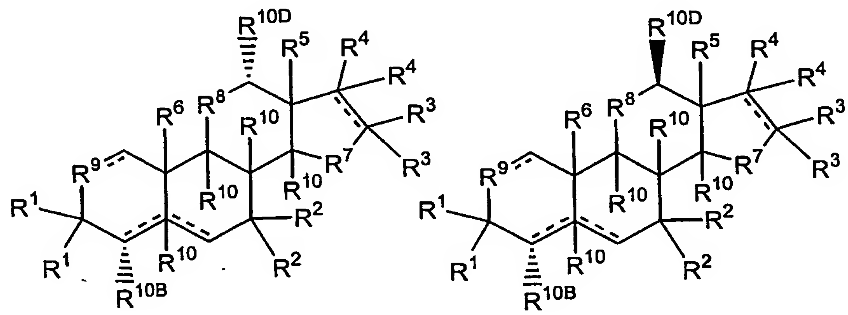

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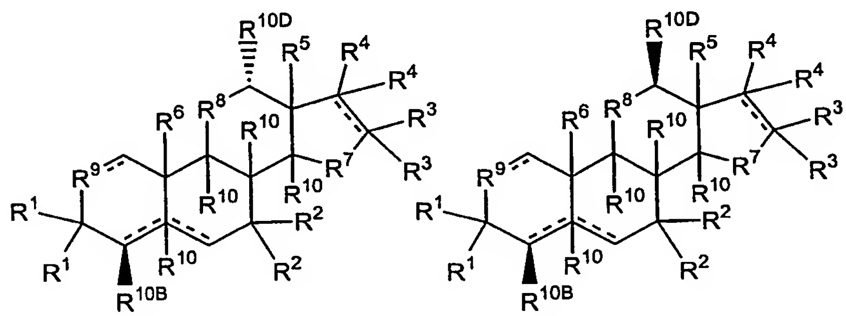

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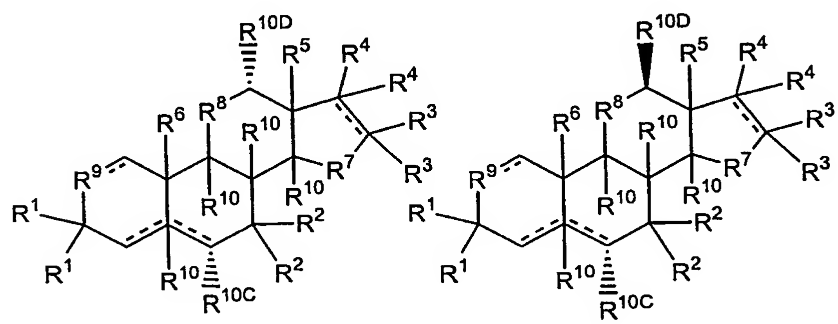
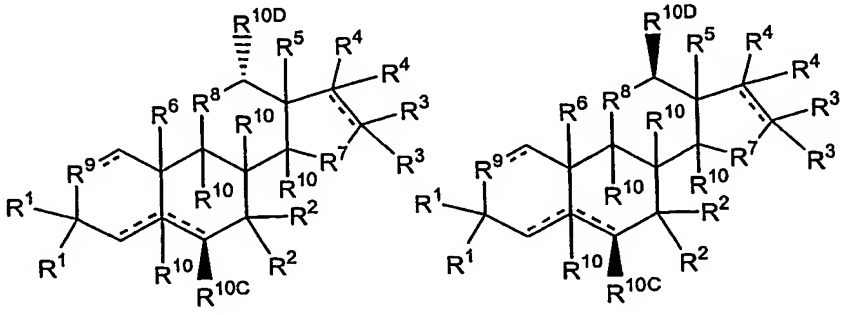


[00973]

AMENDED SHEET

[00974]



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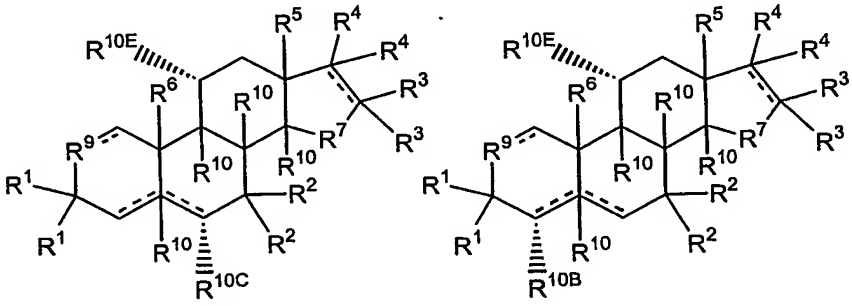

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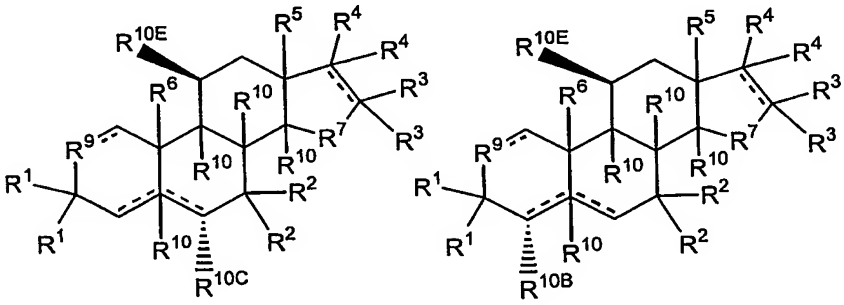

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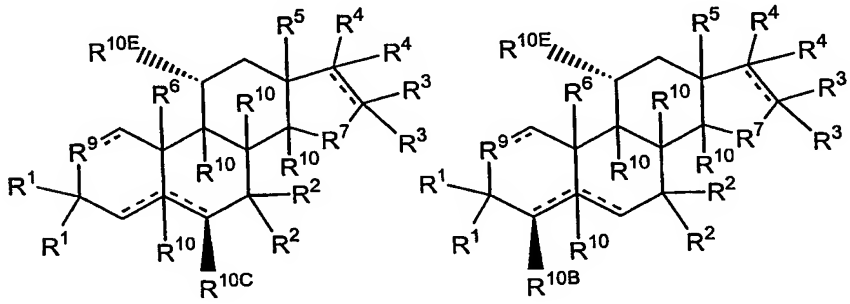
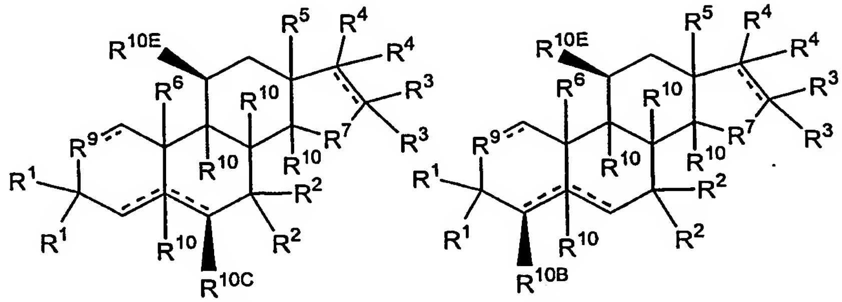


[00978] 

[00979] provided that if a double bond is present at the 1-2, 4-5 or 5-6 positions, then R^{10A}, R^{10B} or R^{10C} respectively are bonded to the ring to which they are linked by a single bond.

[00980] 5. Use according to claim 4 wherein (1) R^5 and R^6 respectively are in the α,α, α,β, β,α or β,β configuration and R^5 and R^6 are optionally both $-CH_3$ or are optionally selected from $-CH_3$ and $-CH_2OH$ or (2) R^5 and R^6 are both in the β-configuration and R^5 and R^6 are optionally both $-CH_3$ or are optionally $-CH_3$ and $-CH_2OH$.

[00981] 6. Use according to claim 5 wherein R^{10} at the 5, 8, 9 and 14-positions respectively are

[00982] (1) -H, -H, -H, -H;

[00983] (2) -H, -H, halogen (-F, -Cl, -Br or -I), -H;

[00984] (3) -H, -H, -H, -OH;

[00985] (4) -H, -H, halogen (-F, -Cl, -Br or -I), -OH;

[00986] (5) -optionally substituted alkyl (e.g., $-CH_3$, $-CH_2OH$, $-CH_2O$-ester, $-C_2H_5$), -H, -H, -H;

[00987] (6) -optionally substituted alkyl (e.g., $-CH_3$, $-CH_2OH$, $-CH_2O$-ester, $-C_2H_5$), -H, halogen (-F, -Cl, -Br or -I), -H;

[00988] (7) -optionally substituted alkyl (e.g., $-CH_3$, $-CH_2OH$, $-CH_2O$-ester, $-C_2H_5$), -H, -H, -OH;

[00989] (8) -acyl (e.g., $-C(O)-(CH_2)_{0-2}-CH_3$), -H, -H, -H;

[00990] (9) -ester (e.g., acetoxy or propionoxy), -H, -H, -H;

[00991] (10) -ether (e.g., $-O-(CH_2)_{0-2}-CH_3$), -H, -H, -H;

[00992] (11) -ester (e.g., acetoxy, propionoxy, $-O-C(O)-(CH_2)_{1-6}-H$), -H, halogen (e.g., -F, -Cl, -Br), -H;

[00993] (12) -ester (e.g., acetoxy or propionoxy), -H, -H, -OH;

[00994] (13) -H, -H, -H, -acyl (e.g., $-C(O)-(CH_2)_{0-2}-CH_3$);

AMENDED SHEET

[00995] (14) -H, -H, -H, -ester (e.g., acetoxy or propionoxy); or

[00996] (15) -H, -H, -H, -ether (e.g., -O-$(CH_2)_{0-2}$-CH_3, -OCH_3, -OC_2H_5, -OCH_2OH, -OCH_2F, -OCH_2Br, -OCH_2COOH, -OCH_2NH_2, -OCH_2CH_2OH, -OCH_2CH_2F, -OCH_2CH_2Br, -OCH_2CH_2COOH or -$OCH_2CH_2NH_2$).

[00997] 7. Use according to claim 6 wherein R^7 is -CH_2-, -CHOH-, -CH(αR^{10})-, -CH(ester)-, -CH(alkoxy)- or -CH(halogen)- where the hydroxyl, ester or alkoxy group or the halogen atom is present in the α-configuration and the alkoxy group is optionally selected from -OCH_3, -OC_2H_5 and -OC_3H_7 and the halogen atom is -F, -Cl, -Br or -I.

[00998] 8. Use according to claim 7 wherein R^8 is -CH_2-, -CF_2-, -CHOH-, -CH(αR^{10})-, -CH(ester)-, -CH(alkoxy)- or -CH(halogen)- where the hydroxyl, ester or alkoxy group or the halogen atom is present in the α-configuration and the alkoxy group is optionally selected from -OCH_3, -OC_2H_5 and -OC_3H_7 and the halogen atom is -F, -Cl, -Br or -I.

[00999] 9. Use according to claim 1 wherein the formula 1 compound is 16α-bromo-3β-hydroxy-5α-androstan-17-one, 16α-fluoro-3β-hydroxy-5α-androstan-17-one, 16α-chloro-3β-hydroxy-5α-androstan-17-one, 16β-bromo-3β-hydroxy-5α-androstan-17-one, 16β-fluoro-3β-hydroxy-5α-androstan-17-one, 16β-chloro-3β-hydroxy-5α-androstan-17-one, 16α,3β-dihydroxy-5α-androstan-17-one, 16β,3β-dihydroxy-5α-androstan-17-one, 16α,3α-dihydroxy-5α-androstan-17-one, 16β,3α-dihydroxy-5α-androstan-17-one, 16α-bromo-3β-hydroxy-5α-androstan-17-one hemihydrate, 3α-hydroxy-16α-fluoroandrostane-17-one, 3β-hydroxy-16α-fluoroandrostane-17-one, 17α-hydroxy-16α-fluoroandrostane-3-one, 17β-hydroxy-16α-fluoroandrostane-3-one, 17α-hydroxy-16α-fluoroandrostane-4-one, 17β-hydroxy-16α-fluoroandrostane-4-one, 17α-hydroxy-16α-fluoroandrostane-6-one, 17β-hydroxy-16α-fluoroandrostane-6-one, 17α-hydroxy-16α-fluoroandrostane-7-one, 17β-hydroxy-16α-fluoroandrostane-7-one, 17α-hydroxy-16α-fluoroandrostane-11-one, 17β-hydroxy-16α-fluoroandrostane-11-one, 16α-fluoroandrost-5-ene-17-one, 7α-hydroxy-16α-fluoroandrost-5-ene-17-one, 7β-hydroxy-16α-fluoroandrost-5-ene-17-one, 4α-hydroxy-16α-fluoroandrost-5-ene-17-one, 3α-hydroxy-16α-fluoroandrost-5-ene-17-one, 3β-hydroxy-16α-fluoroandrost-5-ene-17-one,4β-hydroxy-16α-fluoroandrost-5-ene-17-one, 6α-hydroxy-16α-fluoroandrost-5-ene-17-one, 6β-hydroxy-16α-fluoroandrost-5-ene-17-one, 11α-

hydroxy-16α-fluoroandrost-5-ene-17-one, 11β-hydroxy-16α-fluoroandrost-5-ene-17-one, 4α,17β-dihydroxy-16α-fluoroandrost-5-ene, 4β,17β-dihydroxy-16α-fluoroandrost-5-ene, 6α,17β-dihydroxy-16α-fluoroandrost-5-ene, 6β,17β-dihydroxy-16α-fluoroandrost-5-ene, 11α,17β-dihydroxy-16α-fluoroandrost-5-ene, 11β,17β-dihydroxy-16α-fluoroandrost-5-ene, 4α,17α-dihydroxy-16α-fluoroandrost-5-ene, 4β,17α-dihydroxy-16α-fluoroandrost-5-ene, 6α,17α-dihydroxy-16α-fluoroandrost-5-ene, 6β,17α-dihydroxy-16α-fluoroandrost-5-ene, 11α,17α-dihydroxy-16α-fluoroandrost-5-ene, 11β,17α-dihydroxy-16α-fluoroandrost-5-ene, 7α,17β-dihydroxy-16α-fluoroandrost-5-ene, 7β,17β-dihydroxy-16α-fluoroandrost-5-ene, 3α,17β-dihydroxy-16α-fluoroandrost-5-ene, 3β,17β-dihydroxy-16α-fluoroandrost-5-ene, 3α,17α-dihydroxy-16α-fluoroandrost-5-ene, 3β,17α-dihydroxy-16α-fluoroandrost-5-ene, 1α,17β-dihydroxy-16α-fluoroandrost-5-ene, 1β,17β-dihydroxy-16α-fluoroandrost-5-ene, 2α,17β-dihydroxy-16α-fluoroandrost-5-ene, 2β,17β-dihydroxy-16α-fluoroandrost-5-ene, 12α,17β-dihydroxy-16α-fluoroandrost-5-ene, 12β,17β-dihydroxy-16α-fluoroandrost-5-ene, 1α,17α-dihydroxy-16α-fluoroandrost-5-ene, 1β,17α-dihydroxy-16α-fluoroandrost-5-ene, 2α,17α-dihydroxy-16α-fluoroandrost-5-ene, 2β,17α-dihydroxy-16α-fluoroandrost-5-ene, 12α,17α-dihydroxy-16α-fluoroandrost-5-ene, 12β,17α-dihydroxy-16α-fluoroandrost-5-ene, 15α,17β-dihydroxy-16α-fluoroandrost-5-ene, 15β,17β-dihydroxy-16α-fluoroandrost-5-ene, 17β,18-dihydroxy-16α-fluoroandrost-5-ene, 17β,19-dihydroxy-16α-fluoroandrost-5-ene, 15α,17α-dihydroxy-16α-fluoroandrost-5-ene, 15β,17α-dihydroxy-16α-fluoroandrost-5-ene, 17α,18-dihydroxy-16α-fluoroandrost-5-ene, 17α,19-dihydroxy-16α-fluoroandrost-5-ene, 16α-fluoroandrost-4-ene-17-one, 7α-hydroxy-16α-fluoroandrost-4-ene-17-one, 7β-hydroxy-16α-fluoroandrost-4-ene-17-one, 3α-hydroxy-16α-fluoroandrost-4-ene-17-one, 3β-hydroxy-16α-fluoroandrost-4-ene-17-one, 4α-hydroxy-16α-fluoroandrost-4-ene-17-one, 4β-hydroxy-16α-fluoroandrost-4-ene-17-one, 6α-hydroxy-16α-fluoroandrost-4-ene-17-one, 6β-hydroxy-16α-fluoroandrost-4-ene-17-one, 11α-hydroxy-16α-fluoroandrost-4-ene-17-one, 11β-hydroxy-16α-fluoroandrost-4-ene-17-one, 4α,17β-dihydroxy-16α-fluoroandrost-4-ene, 4β,17β-dihydroxy-16α-fluoroandrost-4-ene, 6α,17β-dihydroxy-16α-fluoroandrost-4-ene, 6β,17β-dihydroxy-16α-fluoroandrost-4-ene, 11α,17β-dihydroxy-16α-fluoroandrost-4-ene, 11β,17β-dihydroxy-16α-fluoroandrost-4-ene, 4α,17α-dihydroxy-16α-fluoroandrost-

4-ene, 4β,17α-dihydroxy-16α-fluoroandrost-4-ene, 6α,17α-dihydroxy-16α-fluoroandrost-4-ene, 6β,17α-dihydroxy-16α-fluoroandrost-4-ene, 11α,17α-dihydroxy-16α-fluoroandrost-4-ene, 11β,17α-dihydroxy-16α-fluoroandrost-4-ene, 7α,17β-dihydroxy-16α-fluoroandrost-4-ene, 7β,17β-dihydroxy-16α-fluoroandrost-4-ene, 3α,17β-dihydroxy-16α-fluoroandrost-4-ene, 3β,17β-dihydroxy-16α-fluoroandrost-4-ene, 3α,17α-dihydroxy-16α-fluoroandrost-4-ene, 3β,17α-dihydroxy-16α-fluoroandrost-4-ene, 1α,17β-dihydroxy-16α-fluoroandrost-4-ene, 1β,17β-dihydroxy-16α-fluoroandrost-4-ene, 2α,17β-dihydroxy-16α-fluoroandrost-4-ene, 2β,17β-dihydroxy-16α-fluoroandrost-4-ene, 12α,17β-dihydroxy-16α-fluoroandrost-4-ene, 12β,17β-dihydroxy-16α-fluoroandrost-4-ene, 1α,17α-dihydroxy-16α-fluoroandrost-4-ene, 1β,17α-dihydroxy-16α-fluoroandrost-4-ene, 2α,17α-dihydroxy-16α-fluoroandrost-4-ene, 2β,17α-dihydroxy-16α-fluoroandrost-4-ene, 12α,17α-dihydroxy-16α-fluoroandrost-4-ene, 12β,17α-dihydroxy-16α-fluoroandrost-4-ene, 15α,17β-dihydroxy-16α-fluoroandrost-4-ene, 15β,17β-dihydroxy-16α-fluoroandrost-4-ene, 17β,18-dihydroxy-16α-fluoroandrost-4-ene, 17β,19-dihydroxy-16α-fluoroandrost-4-ene, 15α,17α-dihydroxy-16α-fluoroandrost-4-ene, 15β,17α-dihydroxy-16α-fluoroandrost-4-ene, 17α,18-dihydroxy-16α-fluoroandrost-4-ene, 17α,19-dihydroxy-16α-fluoroandrost-4-ene, 3β,17β-dihydroxyandrost-5-ene, 3β-hydroxy-7,17-dioxoandrost-5-ene, 3α-hydroxy-7,17-dioxoandrost-5-ene, 3,17-dioxoandrost-5-ene, 3,17-dioxoandrost-4-ene, 3,17-dioxoandrost-1,4-diene, 3β,7β,17β-trihydroxyandrost-5-ene, 3β,7β,17β-trihydroxyandrostane, 3β,16α-dihydroxy-17-oxoandrostane, 3α,16α-dihydroxy-17-oxoandrostane, 3β,16β-dihydroxy-17-oxoandrostane, 3α,16β-dihydroxy-17-oxoandrostane, 3β,16α,17β-trihydroxyandrostane, 3β,16β,17β-trihydroxyandrostane, 3β,16α,17α-trihydroxyandrostane, 3β,16β,17α-trihydroxyandrostane, 3α,16α,17β-trihydroxyandrostane, 3α,16β,17β-trihydroxyandrostane or an analog of any of the foregoing compounds that is suitably substituted to fall within the scope of the claim.

[001000] 10. Use according to claim 1 or 2 wherein the subject has, or is subject or susceptible to developing, neutropenia.

[001001] 11. Use according to claim 10 wherein the subject is a human and wherein the neutropenia is postinfectious neutropenia, autoimmune neutropenia, chronic idiopathic neutropenia or a neutropenia resulting from or

potentially resulting result from a cancer chemotherapy, chemotherapy for an autoimmune disease, an antiviral therapy, radiation exposure, tissue or solid organ allograft or xenograft rejection or immune suppression therapy in tissue or solid organ transplantation or aging or immunesenescence.

[001002] 12. Use according to claim 11 wherein one R^4 is in the β-configuration or the α-configuration and is $-NH_2$, a substituted amine or an amide, which is optionally selected from $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-NHR^{PR}$, -NH-C(O)-H and -NH-C(O)-optionally substituted alkyl.

[001003] 13. Use according to claim 11 wherein the formula 1 compound is 3β-hydroxy-17β-aminoandrost-5-ene, 3β-hydroxy-16α-fluoro-17β-aminoandrost-5-ene, 3β-hydroxy-16β-fluoro-17β-aminoandrost-5-ene, 3β-hydroxy-16,16-difluoro-17β-aminoandrost-5-ene, 3β,16α-dihydroxy-17β-aminoandrost-5-ene, 3β,16β-dihydroxy-17β-aminoandrost-5-ene, 3β-hydroxy-16,16-dimethyl-17β-aminoandrost-5-ene, an ester or carbonate of any of these compounds or an analog of any of the foregoing compounds where the double bond at the 5-6 position is absent and a hydrogen or other R^{10} moiety is present at the 5-position in the α- or β-configuration and/or wherein the hydroxyl group or ester or carbonate analog at the 3-position is present in the α-configuration.

[001004] 14. Use according to claim 1 wherein the formula 1 compound is 3β-hydroxy-17β-aminoandrost-5-ene and wherein the subject is a human who has, or is subject or susceptible to developing, neutropenia.

[001005] 15. Use according to claim 1 wherein the subject is a human having cystic fibrosis.

[001006] 16. Use according to claim 15, wherein one or more symptoms or syndromes are ameliorated, or wherein the progression of the disease is reduced.

[001007] 17. Use according to claim 16, wherein the one or more symptoms or syndromes are 1, 2, 3 or more of *Staphylococcus*, *Haemophilus influenzae, Pseudomonas* or *Burkholderia* respiratory tract or lung infection or propensity to develop a detectable infection or colonization, coughing, wheezing, cyanosis, bronchiolitis, bronchospasm, pneumothorax, hemoptysis, pancreatic exocrine insufficiency, bronchiectatic lung disease, atelectasis-consolidation, pulmonary edema, increased lung vascular hydrostatic pressure, increased lung vascular permeability, sinusitis, respiratory insufficiency, bronchial wall or

interlobular septa thickening, reduction of forced expiratory volume in 1 second, dyspnea, impaired male fertility, elevated sweat chloride, mucous plugging, tree-in-bud sign, mosaic perfusion pattern, glucose intolerance or abnormal elevation of one or more of IL-4, IL-8, RANTES, neutrophil elastase, eosinophils, macrophages, neutrophils, eosinophil cationic protein or cysteinyl leukotrienes.

[001008] 18. Use according to claim 15, 16 or 17 wherein the formula 1 compound is 16α-bromoepiandrosterone, 16α-bromoepiandrosterone hemihydrate, 16β-bromoepiandrosterone, 16α-hydroxyepiandrosterone, 16β-hydroxyepiandrosterone, 3α,17β-dihydroxyandrostane, 3β,17β-dihydroxyandrostane, 3α,16α,17β-trihydroxyandrostane, 3α,16β,17β-trihydroxyandrostane, 3β,16α,17β-trihydroxyandrostane, 3β,16β,17β-trihydroxyandrostane, or an ester, carbonate or other analog of any of these compounds that can convert to the compound by metabolism or hydrolysis.

[001009] 19. A method to treat or to reduce the severity of a chronic allergy or an atopic disease, or one or more symptoms of the chronic allergy or atopic disease in a subject in need thereof, comprising administering an effective amount of a formula 1 compound of claim 1, wherein

[001010] one R^1 is, or both R^1 together are, -OH, -OR^{PR}, -SR^{PR}, -O-Si-$(R^{13})_3$, -COOH, -OSO_3H, -OPO_3H, =O, =S, an ester, a thioester, a thionoester, a phosphoester, a phosphothioester, a phosphonoester, a phosphiniester, a sulfite ester, a sulfate ester, an amide, an amino acid, a peptide, an ether, a thioether, a carbonate or a carbamate, and the other R^1 is independently chosen; and

[001011] one R^4 is, or both R^4 together are, -OH, -OR^{PR}, -SR^{PR}, -$N(R^{PR})_2$, -O-Si-$(R^{13})_3$, -CHO, -CHS, -CN, -SCN, -NO_2, -NH_2, -COOH, -OSO_3H, -OPO_3H, =O, =S, =N-OH, =N-O-optionally substituted alkyl, an ester, a thioester, a thionoester, a phosphoester, a phosphothioester, a phosphonoester, a phosphiniester, a sulfite ester, a sulfate ester, an amide, an amino acid, a peptide, an ether, a thioether, an acyl group, a thioacyl group, a carbonate or a carbamate, and the other R^4 is independently chosen.

[001012] 20. Use according to claim 19 wherein the compound is 16α-bromoepiandrosterone, 16α-bromoepiandrosterone hemihydrate, 16β-bromoepiandrosterone, 16α-iodoepiandrosterone, 16-oxoepiandrosterone, 16-oxoandrosterone, 3β,16α-dihydroxyandrostane-17-one, 3α,16α-dihydroxyandrostane-17-one, 3β,16β-dihydroxyandrostane-17-one, 3α,16β-

dihydroxyandrostane-17-one, 3β,16α,17β-trihydroxyandrostane, 3α,16α,17β-trihydroxyandrostane, 3β,16β,17β-trihydroxyandrostane, 3α,16β,17β-trihydroxyandrostane, or an analog of any of these compounds that is (1) 2-oxa or 11-oxa substituted, (2) substituted at the 7-position with an α-halogen, β-halogen, α-hydroxyl, β-hydroxyl or oxo moiety, (3) a D-ring homo analog, (4) a 19-nor analog and/or (5) an analog of any of the foregoing compounds that is substituted with an R^{10} substituent disclosed herein.

[001013] 21. Use according to claim 20 wherein the level or activity of IgE in the subject is at least transiently detectably reduced.

[001014] 22. Use according to claim 1 wherein the subject is a human who has a sickle cell disease.

[001015] 23. Use according to claim 22 wherein the treatment reduces (1) the severity of pain during vascular or microvascular occlusions, (2) the severity of vascular or microvascular occlusions or (3) the frquency of vascular or microvascular occlusions.

[001016] 24. Use according to claim 22 or 23 comprising intermittent administration of the formula 1 compound.

[001017] 25. Use according to claim 22, 23 or 24 wherein one R^1 is, or both R^1 together are, -H, -OH, -OR^{PR}, -SR^{PR}, -O-Si-$(R^{13})_3$, -COOH, -OSO_3H, -OPO_3H, =O, =S, an ester, a thioester, a thionoester, a phosphoester, a phosphothioester, a phosphonoester, a phosphiniester, a sulfite ester, a sulfate ester, an amide, an amino acid, a peptide, an ether, a thioether, a carbonate or a carbamate, and the other R^1 is independently chosen; and

[001018] one R^4 is, or both R^4 together are, -OH, -OR^{PR}, -SR^{PR}, -$N(R^{PR})_2$, -O-Si-$(R^{13})_3$, -CHO, -CHS, -CN, -SCN, -NO_2, -NH_2, -COOH, -OSO_3H, -OPO_3H, =O, =S, =N-OH, =N-O-optionally substituted alkyl, an ester, a thioester, a thionoester, a phosphoester, a phosphothioester, a phosphonoester, a phosphiniester, a sulfite ester, a sulfate ester, an amide, an amino acid, a peptide, an ether, a thioether, an acyl group, a thioacyl group, a carbonate or a carbamate, and the other R^4 is independently chosen.

[001019] 26. Use according to claim 25 wherein the compound is 3β,17β-dihydroxyandrost-5-ene, 3β,7β,17β-trihydroxyandrost-5-ene, 3β,17β-dihydroxyandrost-1,5-diene, 3β,7β,17β-trihydroxyandrost-1,5-diene, 3β,17β-dihydroxy-16-haloandrost-5-ene, 3β,7β,17β-trihydroxy-16-haloandrost-5-ene, 16α-

fluoro-17-oxoandrost-5-ene, 3α-hydroxy-16α-fluoro-17-oxoandrost-5-ene, 3β-hydroxy-16α-fluoro-17-oxoandrost-5-ene, 3β,17β-dihydroxy-16α-fluoroandrost-5-ene, 3α,17β-dihydroxy-16α-fluoroandrost-5-ene, 16α-bromoepiandrosterone, 16α-bromoepiandrosterone hemihydrate, 16α-iodoepiandrosterone, 16-oxoepiandrosterone, 16-oxoandrosterone, 3β,16α-dihydroxyandrostane-17-one, 3α,16α-dihydroxyandrostane-17-one, 3β,16β-dihydroxyandrostane-17-one, 3α,16β-dihydroxyandrostane-17-one, 3β,16α,17β-trihydroxyandrostane, 3α,16α,17β-trihydroxyandrostane, 3β,16β,17β-trihydroxyandrostane, 3α,16β,17β-trihydroxyandrostane, or an analog of any of these compounds that is (1) 11-oxa substituted or 2-oxa substituted if no double bond is present at the 1-2 position, (2) substituted at the 7-position with an α-halogen, β-halogen, α-hydroxyl, β-hydroxyl or oxo moiety, (3) a D-ring homo analog, (4) a 19-nor analog and/or (5) an analog of any of the foregoing compounds that is substituted with an R^{10} substituent disclosed herein.

[001020] 27. A method to modulate the expression in a cell of the level of or an activity of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more gene products or gene transcripts in the cell, comprising contacting an effective amount of the compound with the cell under suitable conditions and for a sufficient time to detectably modulate the activity or level of the genes, or gene products in the cell, wherein the compound is a formula 1 compound of claim 1 and the gene products or gene transcripts are selected from USF1, c-Fos, EGR1, Cul1, RIPK2, IκBα, IκBKb, NF-κB1 p50, FCAR, c-Fos/ C/EBPβ, RANTES, ICAM1, TSG (TNFAIP6), IL-2 receptor α, GRO2, GRO3, HO1, Jun B, c-Fos/JunB complex, JunB/ATF3 complex, c-Jun, c-Fos/c-Jun complex, ATF-3, MMP1, TSG-6 (TNFAIP3), AP-1, EGR1, TGFβ, ATF-3/c-Jun complex, c-Fos, MMP3, IL-8, STAT5A, STAT5B, CDKN1A, IFNγ receptor 2 (IFNγR2), T-bet, C reactive protein, immunoglobulin E, an AP-1 family protein, GATA-3, Jak2, Tyk2, stat1, stat3, stat4, stat5, stat6, MIP-1α, MIP-2, IP-10, MCP-1, TNF-α, TNF-β, LT-β, IFN-α, IFN-β, TGF-β1, NF-κB, IL-1α, IL-1β, IL-4, IL-6, IL-10, IL-12 receptor β1, IL-12p35, IL-12p40, IL-23, IL-23 receptor, Nrf2, a Maf protein, a thioredoxin, NQO1, GST, HO 1, SOD2, the catalytic subunit of γGCS, the regulatory subunit of γGCS and xCT.

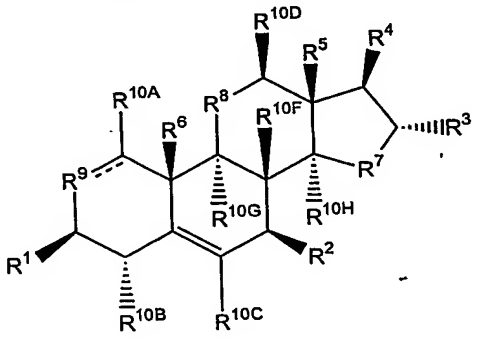
[001021] 28. Use according to claim 27 wherein there is a detectable increase in the level of the mRNA, the protein or one or more biological activities associated with the gene product.

[001022] 29. Use according to claim 27 or 28 wherein the formula 1 compound is 16α-bromo-3β-hydroxy-5α-androstan-17-one, 16α-bromo-3β-hydroxy-5α-androstan-17-one hemihydrate, 16α-fluoro-3β-hydroxy-5α-androstan-17-one, 16α-chloro-3β-hydroxy-5α-androstan-17-one, 16β-bromo-3β-hydroxy-5α-androstan-17-one, 16β-fluoro-3β-hydroxy-5α-androstan-17-one, 16β-chloro-3β-hydroxy-5α-androstan-17-one, 16α,3β-dihydroxy-5α-androstan-17-one, 16β,3β-dihydroxy-5α-androstan-17-one, 16α,3α-dihydroxy-5α-androstan-17-one, 16β,3α-dihydroxy-5α-androstan-17-one, 16α-bromo-3β-hydroxy-5α-androstan-17-one hemihydrate, 3α-hydroxy-16α-fluoroandrostane-17-one, 3β-hydroxy-16α-fluoroandrostane-17-one, 17α-hydroxy-16α-fluoroandrostane-3-one, 17β-hydroxy-16α-fluoroandrostane-3-one, 17α-hydroxy-16α-fluoroandrostane-4-one, 17β-hydroxy-16α-fluoroandrostane-4-one, 17α-hydroxy-16α-fluoroandrostane-6-one, 17β-hydroxy-16α-fluoroandrostane-6-one, 17α-hydroxy-16α-fluoroandrostane-7-one, 17β-hydroxy-16α-fluoroandrostane-7-one, 17α-hydroxy-16α-fluoroandrostane-11-one, 17β-hydroxy-16α-fluoroandrostane-11-one, 16α-fluoroandrost-5-ene-17-one, 7α-hydroxy-16α-fluoroandrost-5-ene-17-one, 7β-hydroxy-16α-fluoroandrost-5-ene-17-one, 4α-hydroxy-16α-fluoroandrost-5-ene-17-one, 3α-hydroxy-16α-fluoroandrost-5-ene-17-one, 3β-hydroxy-16α-fluoroandrost-5-ene-17-one,4β-hydroxy-16α-fluoroandrost-5-ene-17-one, 6α-hydroxy-16α-fluoroandrost-5-ene-17-one, 6β-hydroxy-16α-fluoroandrost-5-ene-17-one, 11α-hydroxy-16α-fluoroandrost-5-ene-17-one, 11β-hydroxy-16α-fluoroandrost-5-ene-17-one, 4α,17β-dihydroxy-16α-fluoroandrost-5-ene, 4β,17β-dihydroxy-16α-fluoroandrost-5-ene, 6α,17β-dihydroxy-16α-fluoroandrost-5-ene, 6β,17β-dihydroxy-16α-fluoroandrost-5-ene, 11α,17β-dihydroxy-16α-fluoroandrost-5-ene, 11β,17β-dihydroxy-16α-fluoroandrost-5-ene, 4α,17α-dihydroxy-16α-fluoroandrost-5-ene, 4β,17α-dihydroxy-16α-fluoroandrost-5-ene, 6α,17α-dihydroxy-16α-fluoroandrost-5-ene, 6β,17α-dihydroxy-16α-fluoroandrost-5-ene, 11α,17α-dihydroxy-16α-fluoroandrost-5-ene, 11β,17α-dihydroxy-16α-fluoroandrost-5-ene, 7α,17β-dihydroxy-16α-fluoroandrost-5-ene, 7β,17β-dihydroxy-16α-fluoroandrost-5-ene, 3α,17β-dihydroxy-16α-fluoroandrost-5-ene, 3β,17β-dihydroxy-16α-fluoroandrost-5-ene, 3α,17α-dihydroxy-16α-fluoroandrost-5-ene, 3β,17α-dihydroxy-16α-fluoroandrost-5-ene, 1α,17β-dihydroxy-16α-fluoroandrost-5-ene, 1β,17β-dihydroxy-16α-fluoroandrost-5-ene, 2α,17β-dihydroxy-16α-fluoroandrost-5-

ene, 2β,17β-dihydroxy-16α-fluoroandrost-5-ene, 12α,17β-dihydroxy-16α-fluoroandrost-5-ene, 12β,17β-dihydroxy-16α-fluoroandrost-5-ene, 1α,17α-dihydroxy-16α-fluoroandrost-5-ene, 1β,17α-dihydroxy-16α-fluoroandrost-5-ene, 2α,17α-dihydroxy-16α-fluoroandrost-5-ene, 2β,17α-dihydroxy-16α-fluoroandrost-5-ene, 12α,17α-dihydroxy-16α-fluoroandrost-5-ene, 12β,17α-dihydroxy-16α-fluoroandrost-5-ene, 15α,17β-dihydroxy-16α-fluoroandrost-5-ene, 15β,17β-dihydroxy-16α-fluoroandrost-5-ene, 17β,18-dihydroxy-16α-fluoroandrost-5-ene, 17β,19-dihydroxy-16α-fluoroandrost-5-ene, 15α,17α-dihydroxy-16α-fluoroandrost-5-ene, 15β,17α-dihydroxy-16α-fluoroandrost-5-ene, 17α,18-dihydroxy-16α-fluoroandrost-5-ene, 17α,19-dihydroxy-16α-fluoroandrost-5-ene, 16α-fluoroandrost-4-ene-17-one, 7α-hydroxy-16α-fluoroandrost-4-ene-17-one, 7β-hydroxy-16α-fluoroandrost-4-ene-17-one, 3α-hydroxy-16α-fluoroandrost-4-ene-17-one, 3β-hydroxy-16α-fluoroandrost-4-ene-17-one, 4α-hydroxy-16α-fluoroandrost-4-ene-17-one, 4β-hydroxy-16α-fluoroandrost-4-ene-17-one, 6α-hydroxy-16α-fluoroandrost-4-ene-17-one, 6β-hydroxy-16α-fluoroandrost-4-ene-17-one, 11α-hydroxy-16α-fluoroandrost-4-ene-17-one, 11β-hydroxy-16α-fluoroandrost-4-ene-17-one, 4α,17β-dihydroxy-16α-fluoroandrost-4-ene, 4β,17β-dihydroxy-16α-fluoroandrost-4-ene, 6α,17β-dihydroxy-16α-fluoroandrost-4-ene, 6β,17β-dihydroxy-16α-fluoroandrost-4-ene, 11α,17β-dihydroxy-16α-fluoroandrost-4-ene, 11β,17β-dihydroxy-16α-fluoroandrost-4-ene, 4α,17α-dihydroxy-16α-fluoroandrost-4-ene, 4β,17α-dihydroxy-16α-fluoroandrost-4-ene, 6α,17α-dihydroxy-16α-fluoroandrost-4-ene, 6β,17α-dihydroxy-16α-fluoroandrost-4-ene, 11α,17α-dihydroxy-16α-fluoroandrost-4-ene, 11β,17α-dihydroxy-16α-fluoroandrost-4-ene, 7α,17β-dihydroxy-16α-fluoroandrost-4-ene, 7β,17β-dihydroxy-16α-fluoroandrost-4-ene, 3α,17β-dihydroxy-16α-fluoroandrost-4-ene, 3β,17β-dihydroxy-16α-fluoroandrost-4-ene, 3α,17α-dihydroxy-16α-fluoroandrost-4-ene, 3β,17α-dihydroxy-16α-fluoroandrost-4-ene, 1α,17β-dihydroxy-16α-fluoroandrost-4-ene, 1β,17β-dihydroxy-16α-fluoroandrost-4-ene, 2α,17β-dihydroxy-16α-fluoroandrost-4-ene, 2β,17β-dihydroxy-16α-fluoroandrost-4-ene, 12α,17β-dihydroxy-16α-fluoroandrost-4-ene, 12β,17β-dihydroxy-16α-fluoroandrost-4-ene, 1α,17α-dihydroxy-16α-fluoroandrost-4-ene, 1β,17α-dihydroxy-16α-fluoroandrost-4-ene, 2α,17α-dihydroxy-16α-fluoroandrost-4-ene, 2β,17α-dihydroxy-16α-fluoroandrost-4-ene, 12α,17α-dihydroxy-16α-fluoroandrost-4-ene, 12β,17α-dihydroxy-16α-

fluoroandrost-4-ene, 15α,17β-dihydroxy-16α-fluoroandrost-4-ene, 15β,17β-dihydroxy-16α-fluoroandrost-4-ene, 17β,18-dihydroxy-16α-fluoroandrost-4-ene, 17β,19-dihydroxy-16α-fluoroandrost-4-ene, 15α,17α-dihydroxy-16α-fluoroandrost-4-ene, 15β,17α-dihydroxy-16α-fluoroandrost-4-ene, 17α,18-dihydroxy-16α-fluoroandrost-4-ene, 17α,19-dihydroxy-16α-fluoroandrost-4-ene, 3β,17β-dihydroxyandrost-5-ene, 3β-hydroxy-7,17-dioxoandrost-5-ene, 3α-hydroxy-7,17-dioxoandrost-5-ene, 3,17-dioxoandrost-5-ene, 3,17-dioxoandrost-4-ene, 3,17-dioxoandrost-1,4-diene, 3β,7β,17β-trihydroxyandrost-5-ene, 3β,7β,17β-trihydroxyandrostane, 3β,16α-dihydroxy-17-oxoandrostane, 3α,16α-dihydroxy-17-oxoandrostane, 3β,16β-dihydroxy-17-oxoandrostane, 3α,16β-dihydroxy-17-oxoandrostane, 3β,16α,17β-trihydroxyandrostane, 3β,16β,17β-trihydroxyandrostane, 3β,16α,17α-trihydroxyandrostane, 3β,16β,17α-trihydroxyandrostane, 3α,16α,17β-trihydroxyandrostane, 3α,16β,17β-trihydroxyandrostane or an analog of any of these compounds that is (1) 11-oxa substituted or 2-oxa substituted if no double bond is present at the 1-2 position, (2) substituted at the 7-position with an α-halogen, β-halogen, α-hydroxyl, β-hydroxyl or oxo moiety, (3) a D-ring homo analog, (4) a 19-nor analog and/or (5) an analog of any of the foregoing compounds that is substituted with an R^{10} substituent disclosed herein.

[001023] 30. A pharmaceutical formulation comprising one or more excipients and a compound having the structure



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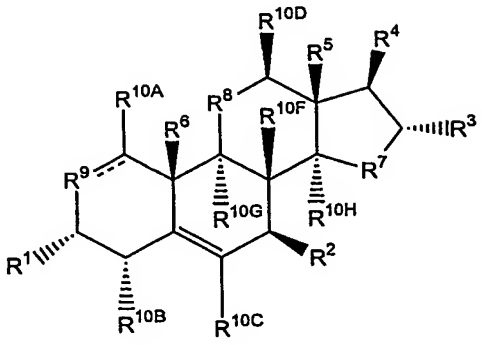
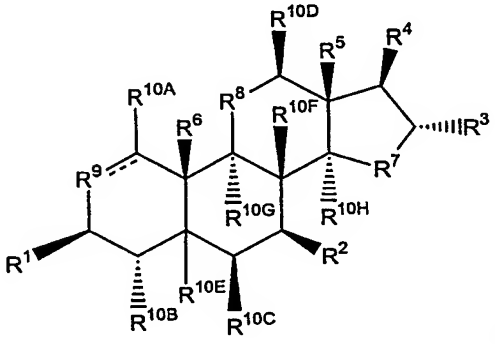
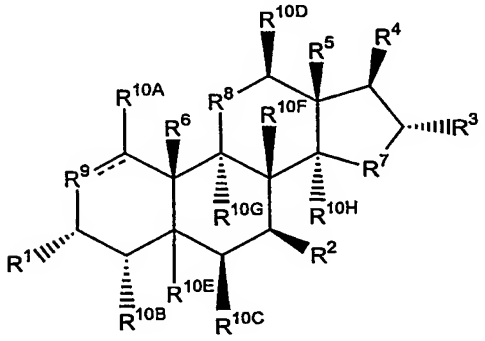
[001025] 

[001026]  or



[001027]

[001028] wherein (1)

[001029] R^1 is -H, -OH, =O, -SH, =S, $-NH_2$ or -NH-C(O)-CH_3, $-CH_3$, ester, ether, thioester, thioether, optionally substituted monosaccharide, optionally substituted oligosaccharide or optionally substituted alkyl;

[001030] R^2 is -H, -OH, =O, -SH, =S, $=CH_2$, $-CH_3$, $-OCH_3$, -F, -Cl, ester, ether, thioester, thioether, optionally substituted monosaccharide, optionally substituted oligosaccharide or optionally substituted alkyl;

[001031] R^3 is -F, -Cl, -Br or -I;

[001032] R^4 is $-NH_2$, $-NHR^{PR}$, -NHOH, -NH-CH_3, =NOH, an amide having the structure -NH-C(O)-optionally substituted alkyl, a carbamate having the structure -NH-C(O)-O-optionally substituted alkyl, a sulfamate having the structure -NH-

S(O)(O)-O-organic moiety, a sulfamide having the structure -NH-S(O)(O)-NH-organic moiety, a sulfonamide having the structure -NH-S(O)(O)-optionally substituted alkyl, a sulfurous diamide or an N-linked amino acid;

[001033] R^5 is $-CH_3$ or $-C_2H_5$;

[001034] R^6 is -H or $-CH_3$;

[001035] R^7 is $-CH_2-$, $-CF_2-$, $-CH_2-CH_2-$, -O-, -S-, -NH-, -CH(α-optionally substituted alkyl), -CH(β-optionally substituted alkyl), -CH(α-OH), -CH(β-OH)- or -C(optionally substituted alkyl)$_2$-;

[001036] R^8 is $-CH_2-$, $-CF_2-$, $-CH_2-CH_2-$, -O-, -S-, -NH-, -CH(α-optionally substituted alkyl), -CH(β-optionally substituted alkyl), -CH(α-OH), -CH(β-OH)- or -C(optionally substituted alkyl)$_2$-;

[001037] R^9 is $-CH_2-$, $-CF_2-$, $-CH_2-CH_2-$, -O-, -S-, -NH-, -N=, -CH(α-optionally substituted alkyl), -CH(β-optionally substituted alkyl), -CH(α-OH), -CH(β-OH)- or -C(optionally substituted alkyl)$_2$-;

[001038] R^{10A}, R^{10B}, R^{10C} and R^{10D} independently are -H, -OH, =O or halogen;

[001039] R^{10E} is in the α-configuration or the β-configuration and is -H or halogen;

[001040] R^{10F} is -H;

[001041] R^{10G} is -H or halogen; and

[001042] R^{10H} is -H, -OH, optionally substituted alkyl or halogen;

[001043] or wherein (2)

[001044] R^1 is -H, -OH, =O, -SH, =S, $-NH_2$ or $-NH-C(O)-CH_3$, $-CH_3$, ester, ether, thioester, thioether, optionally substituted monosaccharide, optionally substituted oligosaccharide or optionally substituted alkyl;

[001045] R^2 is -OH, =O, -SH, =S, $=CH_2$, $-CH_3$, $-OCH_3$, -F, -Cl, ester, ether, thioester, thioether, optionally substituted monosaccharide, optionally substituted oligosaccharide or optionally substituted alkyl;

[001046] R^3 is -H, -OH, =O, -SH, =S, -F, -Cl, -Br, -I, $=CH_2$, ester, ether, thioester, thioether, optionally substituted monosaccharide, optionally substituted oligosaccharide or optionally substituted alkyl;

[001047] R^4 is $-NH_2$, $-NHR^{PR}$, -NHOH, $-NH-CH_3$, =NOH, an amide having the structure -NH-C(O)-optionally substituted alkyl, a carbamate having the structure -NH-C(O)-O-optionally substituted alkyl, a sulfamate having the structure -NH-S(O)(O)-O-organic moiety, a sulfamide having the structure -NH-S(O)(O)-NH-

organic moiety, a sulfonamide having the structure -NH-S(O)(O)-optionally substituted alkyl, a sulfurous diamide or an N-linked amino acid;

[001048] R^5 is $-CH_3$ or $-C_2H_5$;

[001049] R^6 is -H or $-CH_3$;

[001050] R^7 is $-CH_2-$, $-CF_2-$, $-CH_2-CH_2-$, -O-, -S-, -NH-, -CH(α-optionally substituted alkyl), -CH(β-optionally substituted alkyl), -CH(α-OH), -CH(β-OH)- or -C(optionally substituted alkyl)$_2$-;

[001051] R^8 is $-CH_2-$, $-CF_2-$, $-CH_2-CH_2-$, -O-, -S-, -NH-, -CH(α-optionally substituted alkyl), -CH(β-optionally substituted alkyl), -CH(α-OH), -CH(β-OH)- or -C(optionally substituted alkyl)$_2$-;

[001052] R^9 is $-CH_2-$, $-CF_2-$, $-CH_2-CH_2-$, -O-, -S-, -NH-, -N=, -CH(α-optionally substituted alkyl), -CH(β-optionally substituted alkyl), -CH(α-OH), -CH(β-OH)- or -C(optionally substituted alkyl)$_2$-;

[001053] R^{10A}, R^{10B}, R^{10C} and R^{10D} independently are -H, -OH, =O or halogen;

[001054] R^{10E} is in the α-configuration or the β-configuration and is -H or halogen;

[001055] R^{10F} is -H;

[001056] R^{10G} is -H or halogen; and

[001057] R^{10H} is -H, -OH, optionally substituted alkyl or halogen.

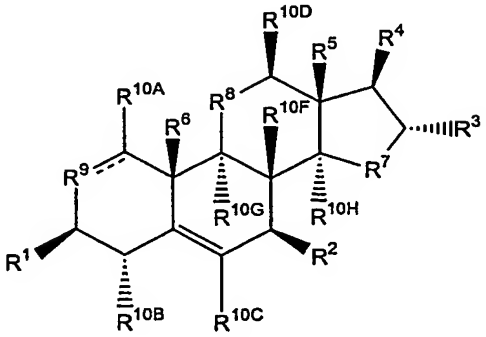
[001058] 31. The pharmaceutical formulation of claim 30 wherein R^2 is -OH, =O, -SH, =S, $=CH_2$, $-CH_3$, $-OCH_3$, -F or -Cl.

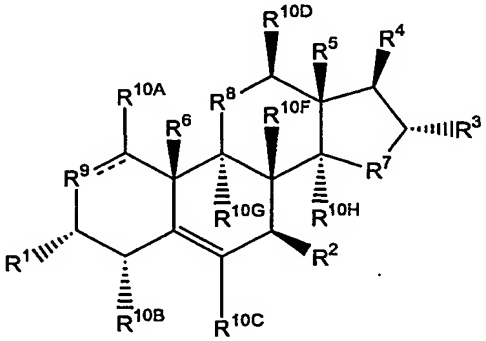
[001059] 32. The pharmaceutical formulation of claim 30 wherein R^6 is -H.

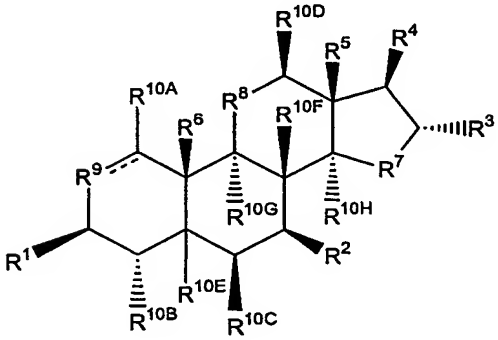
[001060] 33. The pharmaceutical formulation of claim 30 wherein R^{10G} is -F or -Cl.

[001061] 34. The pharmaceutical formulation of claim 30, 31, 32 or 33 wherein R^4 is $-NH_2$ or $-NHR^{PR}$.

[001062] 35. Use of a compound for the treatment of a delayed adverse effect, symptom or condition from ionizing radiation exposure in a subject, wherein the compound has the structure

[001063] 

[001064] 

[001065] 

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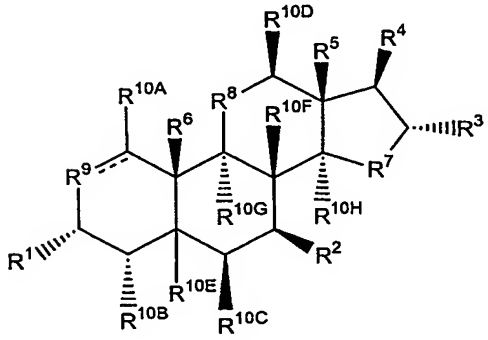
[001066] 

[001067] wherein

[001068] R^1 is -H, -OH, =O, -SH, =S, $-NH_2$ or -NH-C(O)-CH_3, $-CH_3$, ester, ether, thioester, thioether, optionally substituted monosaccharide, optionally substituted oligosaccharide or optionally substituted alkyl;

[001069] R^2 is -H, -OH, =O, -SH, =S, $=CH_2$, $-CH_3$, $-OCH_3$, -F, -Cl, ester, ether, thioester, thioether, optionally substituted monosaccharide, optionally substituted oligosaccharide or optionally substituted alkyl;

[001070] R^3 is -H, -OH, =O, -F, -Cl, -Br, -I, -CN, ester, ether, thioester, thioether, optionally substituted monosaccharide, optionally substituted oligosaccharide or optionally substituted alkyl;

[001071] R^4 is $-NH_2$, $-NHR^{PR}$, -NHOH, -NH-CH_3, =NOH, an amide having the structure -NH-C(O)-optionally substituted alkyl, a carbamate having the structure -NH-C(O)-O-optionally substituted alkyl, a sulfamate having the structure -NH-S(O)(O)-O-organic moiety, a sulfamide having the structure -NH-S(O)(O)-NH-organic moiety, a sulfonamide having the structure -NH-S(O)(O)-optionally substituted alkyl, a sulfurous diamide or an N-linked amino acid;

[001072] R^5 is $-CH_3$ or $-C_2H_5$;

[001073] R^6 is -H or $-CH_3$;

[001074] R^7 is $-CH_2-$, $-CF_2-$, $-CH_2-CH_2-$, -O-, -S-, -NH-, -CH(α-optionally substituted alkyl), -CH(β-optionally substituted alkyl), -CH(α-OH), -CH(β-OH)- or -C(optionally substituted alkyl)$_2$-;

[001075] R^8 is $-CH_2-$, $-CF_2-$, $-CH_2-CH_2-$, -O-, -S-, -NH-, -CH(α-optionally substituted alkyl), -CH(β-optionally substituted alkyl), -CH(α-OH), -CH(β-OH)- or -C(optionally substituted alkyl)$_2$-;

[001076] R^9 is $-CH_2-$, $-CF_2-$, $-CH_2-CH_2-$, -O-, -S-, -NH-, -N=, -CH(α-optionally substituted alkyl), -CH(β-optionally substituted alkyl), -CH(α-OH), -CH(β-OH)- or -C(optionally substituted alkyl)$_2$-;

[001077] R^{10A}, R^{10B}, R^{10C} and R^{10D} independently are -H, -OH, =O or halogen;

[001078] R^{10E} is in the α-configuration or the β-configuration and is -H or halogen;

[001079] R^{10F} is -H;

[001080] R^{10G} is -H or halogen; and

[001081] R^{10H} is -H, -OH, optionally substituted alkyl or halogen.

[001082] 36. Use according to claim 35 wherein the subject is a human or another primate and the delayed adverse effect, symptom or condition is fever,

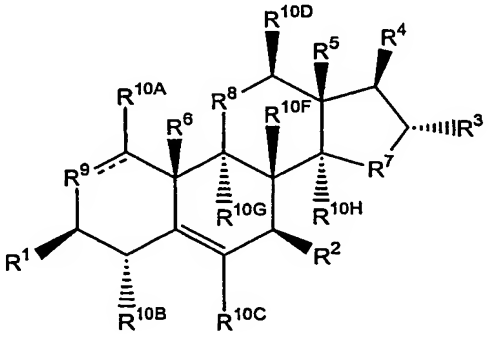
pain, radiation-induced enteritis or diarrhea, pseudomembranous inflammation, perivascular fibrosis, endothelial cell damage or death, cardiac tissue inflammation or damage or pericardial disease, pulmonary tissue inflammation or damage, hematopoietic or marrow cell inflammation or damage, endocrine or thyroid dysfunction, decreased growth or decreased bone development or density, central nervous system inflammation or damage, connective tissue damage, gastric ulceration or small bowel obstruction or fistula formation.

[001083] 37. Use according to claim 35 or 36 wherein the compound is 3β-hydroxy-17β-aminoandrost-5-ene or a 2-oxa, 2-aza, 11-oxa, 11-aza, 9-halogen, 16-halogen, 16-hydroxyl, 16-oxo, or 19-nor analog thereof.

[001084] 38. Use according to claim 37 wherein the compound is 3β-hydroxy-17β-aminoandrost-5-ene.

[001085] 39. Use of a compound for the treatment of an immune suppression condition or an unwanted inflammation or autoimmune condition in a subject, wherein the compound has the structure

[001086]



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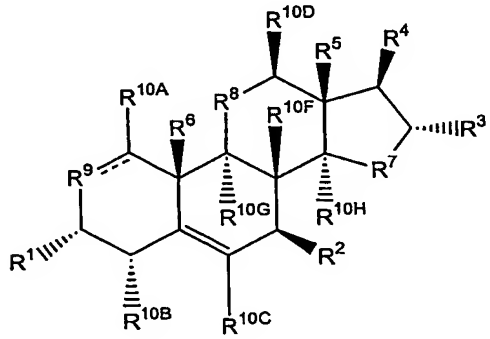

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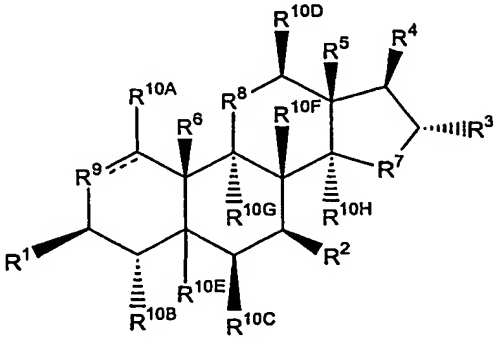

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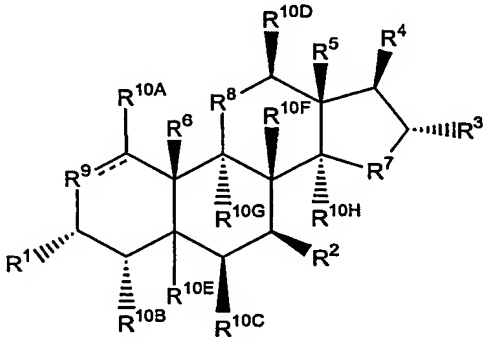

[001089]

[001090] wherein

[001091] R^1 is -H, -OH, =O, -SH, =S, $-NH_2$ or -NH-C(O)-CH_3, $-CH_3$, ester, ether, thioester, thioether, optionally substituted monosaccharide, optionally substituted oligosaccharide or optionally substituted alkyl;

[001092] R^2 is -H, -OH, =O, -SH, =S, $=CH_2$, $-CH_3$, $-OCH_3$, -F, -Cl, ester, ether, thioester, thioether, optionally substituted monosaccharide, optionally substituted oligosaccharide or optionally substituted alkyl;

[001093] R^3 is -H, -OH, =O, -F, -Cl, -Br, -I, -CN, ester, ether, thioester, thioether, optionally substituted monosaccharide, optionally substituted oligosaccharide or optionally substituted alkyl;

[001094] R^4 is $-NH_2$, $-NHR^{PR}$, -NHOH, -NH-CH_3, =NOH, an amide having the structure -NH-C(O)-optionally substituted alkyl, a carbamate having the structure -NH-C(O)-O-optionally substituted alkyl, a sulfamate having the structure -NH-S(O)(O)-O-organic moiety, a sulfamide having the structure -NH-S(O)(O)-NH-organic moiety, a sulfonamide having the structure -NH-S(O)(O)-optionally substituted alkyl, a sulfurous diamide or an N-linked amino acid;

[001095] R^5 is $-CH_3$ or $-C_2H_5$;

[001096] R^6 is -H or $-CH_3$;

[001097] R^7 is $-CH_2-$, $-CF_2-$, $-CH_2-CH_2-$, -O-, -S-, -NH-, -CH(α-optionally substituted alkyl), -CH(β-optionally substituted alkyl), -CH(α-OH), -CH(β-OH)- or -C(optionally substituted alkyl)$_2$-;

[001098] R^8 is $-CH_2-$, $-CF_2-$, $-CH_2-CH_2-$, -O-, -S-, -NH-, -CH(α-optionally substituted alkyl), -CH(β-optionally substituted alkyl), -CH(α-OH), -CH(β-OH)- or -C(optionally substituted alkyl)$_2$-;

[001099] R^9 is $-CH_2-$, $-CF_2-$, $-CH_2-CH_2-$, -O-, -S-, -NH-, -N=, -CH(α-optionally substituted alkyl), -CH(β-optionally substituted alkyl), -CH(α-OH), -CH(β-OH)- or -C(optionally substituted alkyl)$_2$-;

[001100] R^{10A}, R^{10B}, R^{10C} and R^{10D} independently are -H, -OH, =O or halogen;

[001101] R^{10E} is in the α-configuration or the β-configuration and is -H or halogen;

[001102] R^{10F} is -H;

[001103] R^{10G} is -H or halogen; and

[001104] R^{10H} is -H, -OH, optionally substituted alkyl or halogen.

[001105] 40. Use according to claim 39 wherein the subject is a human or another primate and the immune suppression condition is an innate immune suppression condition or immunosenesence.

[001106] 41. Use according to claim 40 wherein the unwanted inflammation or autoimmune condition is rheumatoid arthritis, osteoarthritis, psoriatic arthritis, polyarthritis, osteoporosis, an allergy, multiple sclerosis, dermatitis, autoimmune glomerulonephritis, systemic lupus erythematosus, autoimmune pulmonary inflammation, asthma, ischemia-reperfusion injury, inflammatory bowel disease, regional enteritis, ulcerative colitis or Crohn's disease.

[001107] 42. Use according to claim 39, 40 or 41 wherein the compound is 3β-hydroxy-17β-aminoandrost-5-ene or a 2-oxa, 2-aza, 11-oxa, 11-aza, 9-halogen, 16-halogen, 16-hydroxyl, 16-oxo, or 19-nor analog thereof.

[001108] 43. Use according to claim 42 wherein the compound is 3β-hydroxy-17β-aminoandrost-5-ene.

[001109] 44. Use of a compound of claim 30 for the preparation of a medicament.